

Synthesis and Characterization of Novel Isosorbide-Based Polyester Derivatives Decorated with α -Acyloxy Amides

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The synergy of multicomponent reactions (MCRs) and metathesis chemistry is applied for the synthesis of bio-based functional isosorbide polymers (i.e., polyesters) decorated with α -acyloxy amide motif. The chemical structure of the polyesters that are not accessible by any other conventional methodologies is characterized in-depth via nuclear magnetic resonance, size-exclusion chromatography, and attenuated total reflectance infrared spectroscopy. It is also observed that the “biomass-derived” carbon % of the polymers varied between 66.2 and 76.9. Moreover, the thermal properties of the novel isosorbide-based polymers are investigated via thermogravimetric analysis and differential scanning calorimetry, revealing that the polymers are in the amorphous state, identified by the glass transition temperature (T_g) values below the human body temperature. The mechanical properties and the biocompatibility of the functional novel polyester derivative with the highest “biomass-derived” carbon % are evaluated via dynamic mechanical analysis and cytotoxicity test. The exemplary polymer is biocompatible with chondrocyte cells in the conditions used in the tests. In summary, the complementary nature of isosorbide derivatives with MCRs and metathesis chemistry is utilized to illustrate the potential utility of isosorbide as a building block for polymers with prospective biomedical application (namely, as novel cartilage materials).

Particularly, isosorbide derived polymers are anticipated to (partially) avoid the use of fossil resources and address additional global issues, such as pollution based on synthetic plastics and increasing piles of waste streams of different industrial origins. Isosorbide has been recognized as a direct replacement for rigid diols like bisphenol A.^[2] Accordingly, isosorbide has been employed in diverse polymerization methods, the step-growth polymerization being the most common utilized, to create bio-based polymers with excellent properties (such as strong resistance to UV irradiation, heat, chemical degradation, impact, and abrasion along optical clarity).^[3,4] The obtained polymers, hence, have witnessed a broad array of applications (e.g., from packaging to automobile parts and biomedical devices). Inevitably, several reviews highlight the importance of isosorbide in the field of polymer chemistry and materials science.^[5] Nevertheless, the direct use of isosorbide in step-growth polymerization is still challenging due to the low and disparate reactivity of the secondary hydroxyl groups. Thus, novel synthetic

approaches that circumvent the hydroxyl group reactivity issue are of major interest for the preparation of tailored polymers. The latter is feasible by increasing the reactivity of isosorbide in step-growth polymerizations through functionalization of the secondary alcohol units to more reactive units, such as alkyne,

1. Introduction

Isosorbide (1,4:3,6-dianhydrosorbitol), which is a rigid bicyclic compound directly derived from glucose, is receiving ever growing interest both industrially and academically.^[1]

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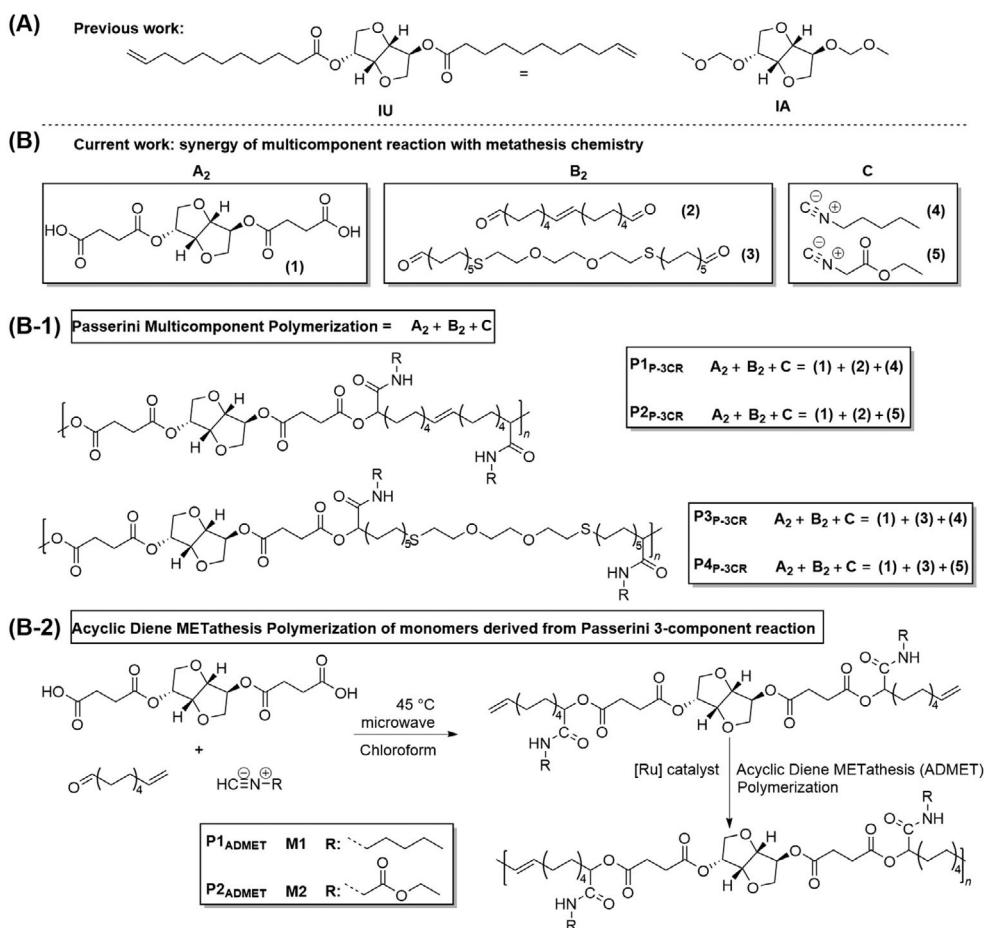
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DOI: 10.1002/macp.202100497



Scheme 1. Schematic representation of: A) previously reported isosorbide undecenoate (IU) and a bis-methoxymethyl isosorbide acetal (IA), as examples of isosorbide derivatives polymerizable via unconventional step-growth polymerization methods; B) current work which is based on the synergy of multicomponent reaction with metathesis chemistry; hence, depicting the starting materials essential for the approach; B-1) the Passerini three-component reaction (P-3CR) as a highly efficient and atom-economic step-growth polymerization approach (i.e., $A_2 + B_2 + C$) to deliver functional polyesters decorated with α -acyloxy amides $P1_{P-3CR}$ – $P4_{P-3CR}$ by using a dicarboxylic acid (1) as A_2 , dialdehydes (2) or (3) as B_2 , and isocyanides (4) or (5) as C, respectively; B-2) the synthesis of a new tailor-made α,ω -diene functionalized isosorbide monomers M1 and M2 via Passerini 3-component reaction, and their subsequent polymerization via ADMET chemistry to afford polymer $P1_{ADMET}$ and $P2_{ADMET}$, respectively.

azide, and alkene.^[1] Acyclic diene metathesis (ADMET) polymerization, as an unconventional step-growth polymerization method,^[6] has been a method of choice for the polymerization of isosorbide undecenoate (IU shown in **Scheme 1A**) to yield aliphatic polyesters with number average molecular masses ranging from 9000 to 51 000 g mol⁻¹.^[7] It is important to mention that IU is derived from coupling isosorbide with a castor oil^[8] derivative, that is, 10-undecenoic acid. Alternatively, a bis-methoxymethyl acetal derivative of isosorbide (IA in **Scheme 1A**) was polymerized by using the 2–5 mol% of *p*-toluenesulfonic acid via an acetal metathesis polymerization.^[9] This method, as well as ADMET polymerization, are polycondensations in which the removal of molecules with low boiling point is the driving force for the polymerization. Aside, the IU was also polymerized by polyaddition using the efficient, 100% atom economic thiol–ene “click” reaction. Particularly, the thiol–ene miniemulsion polymerization was employed with 1,4-butanethiol to deliver poly(ester-thioether)s as analogues to the previously described ADMET polyesters derivatives.^[10]

Although substantial advances have been implemented toward new step-growth techniques to incorporate isosorbide into polymers, creative synthesis approaches are still essential as a driving force for future innovations and applications of tailor-made polymers from isosorbide. Compared with the traditional two-monomer polycondensation methods, polymerizations based on multicomponent reactions (MCRs),^[11] in which at least three functional groups are involved, have attracted significant attention in the fields of polymer chemistry and materials science. Multicomponent polymerizations (MCPs) constitute a straightforward method to synthesize complex polymers with structural diversity in a highly atom- and step-economic manner. Novel polymers with predictable topological structures using different monomers were synthesized from the metal-free Passerini three component reaction (P-3CR), in which a carboxylic acid reacts with a ketone or an aldehyde in the presence of an isocyanide to yield an α -acyloxy amide motif.^[12] The P-3CR can extensively expand the versatility of the isosorbide-based polymers via the diverse combinations of at least three monomers.

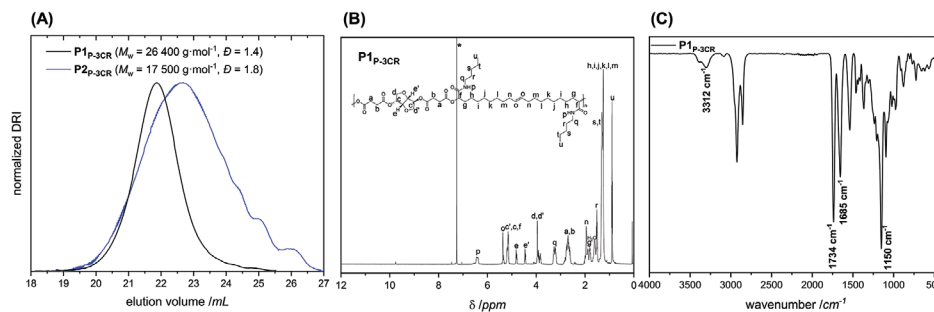


Figure 1. A) Comparative SEC of the isocyanide-based multicomponent polymers P1_{P-3CR} (black line, $M_w = 26\,400\text{ g mol}^{-1}$, $\bar{D} = 1.4$) and P2_{P-3CR} (blue line, $M_w = 17\,500\text{ g mol}^{-1}$, $\bar{D} = 1.8$). B) ^1H NMR (500 MHz, CDCl_3) spectrum of P1_{P-3CR}. C) ATR-IR spectra of P1_{P-3CR}.

We herein report the synthesis of partially bio-based functional isosorbide polymers (i.e., polyesters) with distinctive properties using the P-3CR. The P-3CR was employed either as a direct polymerization approach or as a handle for the synthesis of novel isosorbide monomers, which are further polymerized via ADMET polymerization. Both approaches rely on the utilization of diacid derivative of isosorbide which is obtained via the cyclic anhydride functionalization. The α -acyloxy amide motive features an ester moiety alongside an amide moiety as is characteristic for depsipeptides.^[13] Accordingly, the influence of the electron-withdrawing α -acyloxy amide functional group on the thermal properties of the novel isosorbide-based polymers was investigated. Since isosorbide decorated polyesters are mainly used in biomedical applications, it was important to ensure the mechanical properties along the biocompatibility of the functional novel polyester derivatives. Therefore, dynamic mechanical analysis (DMA) and cytotoxicity test were performed on an exemplary polymer, which also possessed the highest “biomass-derived” carbon % (76.9%).

2. Results and Discussion

In the seminal work of Meier et al.,^[12] the P-3CR was adopted as a highly efficient and atom-economic step-growth polymerization approach (i.e., $A_2 + B_2 + C$) to deliver functional polyesters by using a dicarboxylic acid, a dialdehyde, and an isocyanide (Scheme 1B). Thus, in the current work, isosorbide-derived diacid (A_2) and easily accessible castor oil-derived dialdehydes (B_2) were designed as the difunctional monomers, while commercially available isocyanide derivatives were chosen as the monofunctional monomer (i.e., C) (Scheme 1B). Indeed, the most effective method to modify the less reactive secondary hydroxyl functionality of the isosorbide was to chemically convert them into active functional groups such as carboxylic acids, thus to deliver isosorbide-derived diacid (A_2).^[1] Importantly, the cyclic anhydride (e.g., succinic) functionalization is a common method to enhance the reactivity of isosorbide.^[14,15] Thus, the previously reported microwave mediated condensation of isosorbide and succinic anhydride^[14] was used to deliver the corresponding diacid (**1**) in Scheme 1B) in quantitative yield under solvent-free conditions (see Section C1 in the Supporting Information for details on the synthesis). The chemical structure of (**1**) was verified by nuclear magnetic resonance (NMR) (compare Figures S1–S3, Supporting Information) and attenuated total reflection (ATR)-

mode Fourier transform infrared (ATR-IR) analysis (Figure S4, Supporting Information). The respective analytical data was in accordance with the one reported in the literature.^[14] It is important to mention that succinic anhydride was identified as an ideal co-starting material by virtue of the considerable progress toward the synthesis of bio-succinic acid at a competitive price.^[16] To deliver the second building block (i.e., B_2) for the multicomponent polymerization reaction, 10-undecenal, which can be obtained by pyrolysis and reduction of castor oil, was efficiently transformed into the corresponding C_{20} dialdehyde (**2**) via self-metathesis reaction in the presence of Hoveyda–Grubbs second generation (HG II) as a catalyst (refer to Section C2 in the Supporting Information and Figures S5 and S6, Supporting Information).^[17] Alternatively, a novel dialdehyde (**3**) shown in Scheme 1B was prepared via light-induced thiol–ene addition of 10-undecenal and 3,6-dioxa-1,8-octanedithiol in the presence of 2,2-dimethoxy-2-phenylacetophenone as radical initiator at 320 nm (Section C3 in the Supporting Information). The successful synthesis of (**2**) and (**3**) was affirmed via detailed NMR characterization. On the one hand, the NMR data for (**2**) was in agreement with the literature.^[18] On the other hand, ^1H -NMR analysis of (**3**) has revealed that the magnetic resonances at 5.74 and 4.91 ppm corresponding to the terminal double bond of 10-undecenal have disappeared, whereas the peak at 9.76 ppm, resulting from the aldehyde functional group, has remained intact (Figure S7, Supporting Information). Additionally, new triplets at 2.78 and 2.62 ppm corresponding to the protons at the α - and β -positions to the thioether arose. Having established the essential components for the isocyanide-based multicomponent polymerization (e.g., the isosorbide-derived diacid (**1**) as A_2 and castor oil-derived dialdehydes (**2**) and (**3**) as B_2), the first polymerization attempt to deliver isosorbide-derived polyesters containing α -acyloxy amide groups (i.e., P1_{P-3CR}) was performed with (**1**) and (**2**) in the presence of commercially available 1-pentyl isocyanide (**4**) as monomer C at molar ratio of 1:1:2 according the stoichiometric balance. In line with previously well-documented results,^[19] the polymerization was carried out in an aprotic solvent (i.e., CHCl_3) at 45 °C under microwave (μm)-radiation. As expected, high monomer concentration (2 M) and long polymerization time (96 h) favored reasonable polymer yield ($\approx 89\%$) and weight average molar mass (M_w). The obtained polymer was precipitated in ice cold methanol, and accordingly, size-exclusion chromatography (SEC) measurement in THF as eluent displayed a M_w of $26\,400\text{ g mol}^{-1}$, and a dispersity (\bar{D}) of 1.4 for polymer P1_{P-3CR} (compare Figure 1A (black line) and Table 1, Entry 1).

Table 1. Polymerization and thermal data along information on the renewable source atom content (i.e., “biomass-derived” carbon) percentage of the polyester derivatives decorated with α -acyloxy amides, that is, P1_{P-3CR}–P4_{P-3CR} and P1_{ADMET} and P2_{ADMET}, respectively.

Polymer	M_w [g mol ⁻¹] SEC ^{a)}	\bar{D} [M_w/M_n] SEC ^{a)}	$T_{d,5\%}$ [°C] TGA	T_g [°C] DSC	Isolated yields [%]	Renewable source atom content [%]
P1 _{P-3CR}	26 400	1.4	249	9	65	73.5
P2 _{P-3CR}	17 500	1.8	313	22	82	76.9
P3 _{P-3CR}	10 000	1.4	225	-11	33	63.9
P4 _{P-3CR}	17 800	2.2	288	-6	71	66.6
P1 _{ADMET}	26 700	1.7	248	13	45	73.5
P2 _{ADMET}	37 800	2.1	313	22	87	76.9

^{a)} M_w and \bar{D} values are of the precipitated polymers.

In order to confirm the polymer structure, P1_{P-3CR} was characterized by NMR measurement. The relative proton signals (f and g at 5.22 and 1.75 ppm, respectively) of α -acyloxy amide moieties that should be generated via the expected Passerini polymerization reaction could be clearly observed in the ¹H NMR spectrum of P1_{P-3CR} (Figure 1B). In line, the disappearance of magnetic resonances (i.e., 9.76 ppm) of the aldehyde functional unit was also observed. Aside, with the appearance of the corresponding peak in the ¹³C NMR spectrum (74.5 ppm), the proposed chemical structure of P1_{P-3CR} was also proved (compare Figure S16, Supporting Information). Along with the NMR measurements, the attenuated total reflection (ATR)-mode Fourier transform infrared (ATR-IR) recordings of the obtained P1_{P-3CR} revealed the distinctive bands of ester and amide C=O stretching, respectively, at 1734 and 1685 cm⁻¹, in addition to the N–H stretch of the α -acyloxy amide at 3312 cm⁻¹ (Figure 1C). Aside, the absorption at 1150 cm⁻¹ could be ascribed to the stretching vibration of –C–O–C bonds, which indicated the presence of isosorbide moiety within the polymer. Importantly, the absence of the carbon–hydrogen stretching peak of the –CHO around 2820 and 2720 cm⁻¹ in the ATR-IR spectra of the P1_{P-3CR} has implied that the aldehyde group in (2) has been reacted and a high degree of polymerization was achieved. The reproducibility and the versatility of the Passerini-3CR syntheses were assessed by reacting (1) and (2) with different aliphatic isocyanide (i.e., ethyl isocyanacetate, (5)) under the above-mentioned reaction conditions (e.g., 2 M, 45 °C, μ M-radiation, 96 h) to generate polymer P2_{P-3CR} (M_w = 17 500 g mol⁻¹, \bar{D} = 1.8; compare Figure 1A (blue line) and Table 1, Entry 2). In similar manner, (1) was reacted with the castor oil-derived dialdehyde (3) in the presence of either 1-pentyl isocyanide (4) or ethyl isocyanacetate (5) to deliver polymers P3_{P-3CR} (M_w = 10 000 g mol⁻¹, \bar{D} = 1.4) and P4_{P-3CR} (M_w = 17 800 g mol⁻¹, \bar{D} = 2.2), respectively as it is depicted in Table 1. In general, all Passerini-3CR polymerizations (P2_{P-3CR}–P4_{P-3CR}) proceeded with varied monomer combination, affording soluble products, whose chemical structures were characterized by NMR and IR spectroscopy (refer to Section C8 in the Supporting Information).

The combination of the MCRs (e.g., the Passerini-3CR) and step-growth polymerization (i.e., ADMET) has been successfully employed to synthesize novel polymers which are not otherwise easily accessible.^[20] ADMET polymerization is an efficient

approach for the polymerization of α,ω -diene monomers. By virtue of the plethora of modern ruthenium-based metathesis catalysts, which are tolerant to manifold of functional groups, diverse α,ω -dienes were successfully polymerized via ADMET polymerization.^[6] Thus, the Passerini-3CR was alternatively applied to synthesize, in a one-step procedure, novel α,ω -dienes containing an isosorbide core and different substituents at the amide moiety (Scheme 1, B-2). Particularly, castor oil-based 10-undecenal was reacted with (1) and an isocyanide derivative (either 1-pentyl isocyanide (4) or ethyl isocyanacetate (5)) to afford α,ω -diene monomers M1 and M2, respectively, by stirring the components in CHCl₃ at 45 °C for 2 days (Scheme 1, B-2). After purification by column chromatography, pure M1 and M2 were isolated in yield of 36% and 58%, respectively. The chemical structure of the monomers was extensively characterized by NMR spectroscopy (compare Figures S9–S14, Supporting Information). Subsequently, the behavior of the synthesized α,ω -dienes in the ADMET polymerization was investigated. Based on previous results,^[21] the ADMET polymerization of the Passerini monomers was performed in the presence of HG II (2.0 mol%/molecule) as catalyst at 65 °C with *o*-dichlorobenzene as solvent for 3 h (Scheme 1, B-2). The polymerization reaction was carried out under dynamic vacuum (200 mbar → 0 mbar) in order to ensure the formation of high molecular weight polymers P1_{ADMET} (R = pentyl) and P2_{ADMET} (R = ethyl acetate), respectively, from monomer M1 and M2. Eventually, the SEC analysis of the polymers confirmed the polymer formation with M_w of 26 700 g mol⁻¹ (\bar{D} = 1.7) and 37 800 g mol⁻¹ (\bar{D} = 2.1) for P1_{ADMET} and P2_{ADMET}, respectively (Figure 2A). It should be noted here that the chemical nature of the repeating unit of these polymers are identical compared to that of the polymers P1_{P-3CR} – P2_{P-3CR} (although the distinguishable values for the apparent molecular weight and dispersity), the latter being confirmed via NMR and ATR-IR (Figure 2B, and refer to Figures S15–S19, Supporting Information). The fraction of “biomass-derived” carbon in the synthesized functional polyesters was assessed by calculating the percentage of carbon in the polymer that was bio-based, revealing that the “biomass-derived” carbon % varied between 66.2 and 76.9, being the highest for P2_{ADMET} (P2_{P-3CR}).

As previously mentioned, isosorbide undecenoate (α,ω -diene shown in Scheme 1A) was polymerized directly via ADMET polymerization to yield semi-crystalline unsaturated aliphatic polyester (i.e., PIU) with decomposition temperature (at 5% weight loss), $T_{d,5\%}$, of 369 °C, glass transition temperature, T_g , of -10 °C and melting point temperature, T_m , of 38 °C.^[7b] Consistently, it was of crucial importance to determine the impact on the thermal properties of the α -acyloxyamide moiety. As shown in Table 1 and Figure 2C, all polymers displayed reasonable thermostability with, for instance, $T_{d,5\%}$ of 248 °C (P1_{ADMET}) and 313 °C (P2_{ADMET}) under inert conditions (i.e., nitrogen). The polymerization approach (e.g., Passerini-3CR polymerization or ADMET) does not have impact on the thermal stability of the polymers, as $T_{d,5\%}$ of P1_{ADMET} and P1_{P-3CR}, on the one hand, and P2_{ADMET} and P2_{P-3CR} were similar. The nature of the acyloxyamide substituent impacted the polymer thermal stability. The polymers featuring an ester as pending chain displayed $T_{d,5\%}$ around 60 °C higher than their alkyl group equivalent. This increase in thermal stability could be explained by the presence of hydrogen bonds between the ester and the acyloxy amide moieties. Additionally,

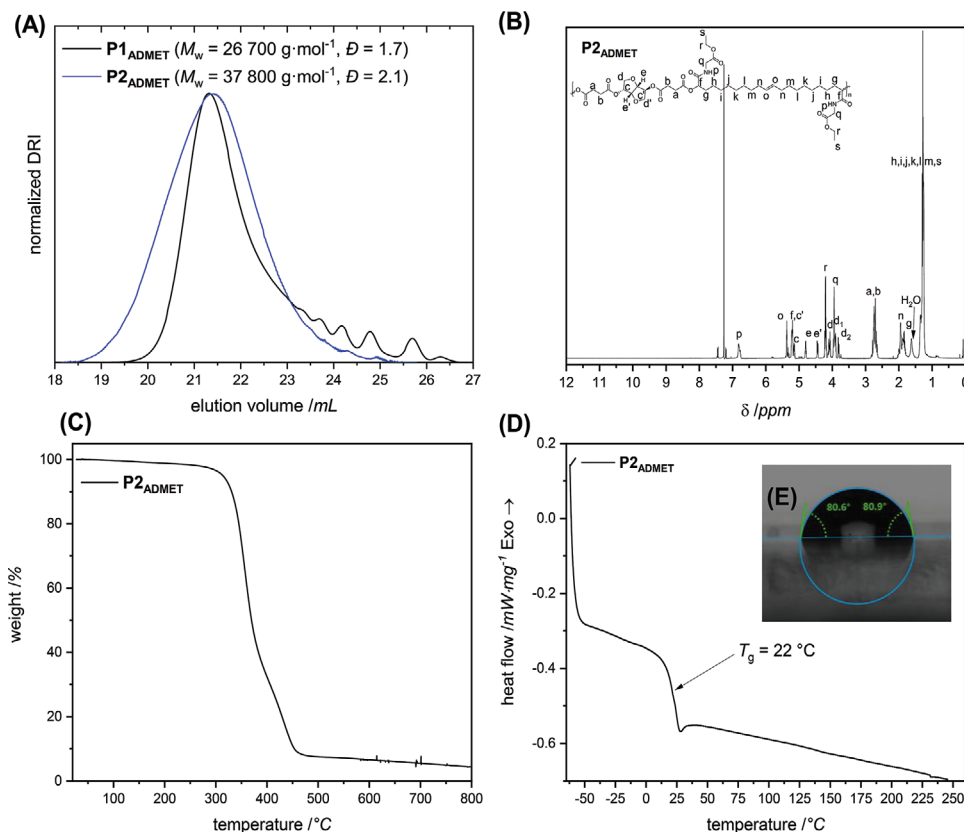


Figure 2. A) Comparative SEC of the ADMET polymers P1_{ADMET} (black line, $M_w = 26\,700\text{ g mol}^{-1}$, $\bar{D} = 1.7$) and P2_{ADMET} (blue line, $M_w = 37\,800\text{ g mol}^{-1}$, $\bar{D} = 2.1$). B) ^1H NMR (500 MHz, CDCl_3) spectrum of P2_{ADMET}. C,D) TGA and DSC data of P2_{ADMET}, respectively, revealing $T_{d,5\%}$ of $313\text{ }^\circ\text{C}$ and T_g of $23\text{ }^\circ\text{C}$. E) Water droplet with a volume of $5\ \mu\text{L}$ on flat film of P2_{ADMET}.

the structure of the aldehyde employed in the MCR reaction influenced the thermal stability of the polymers. The presence of heteroatoms (S and O) in their structure decreased the $T_{d,5\%}$ of around $20\text{ }^\circ\text{C}$ compared to than the polymers with an alkyl chain equivalent.

Contrary to the semi-crystalline morphology reported for PIU, differential scanning calorimetry (DSC) analyses showed that all the polymers prepared by combination of MCR and ADMET were amorphous (Table 1 and Figure 2D).^[15] P1_{ADMET} exhibited lower T_g value ($13\text{ }^\circ\text{C}$) than P2_{ADMET} ($22\text{ }^\circ\text{C}$), due to the fact that the presence of ester moieties induces van der Waals interactions and can form hydrogen bonds with the acyloxy amide moieties. Moreover, the structure of the aldehyde employed in the MCR reaction influences the polymer T_g values. The T_g values of P3_{P-3CR} ($-11\text{ }^\circ\text{C}$) and P4_{P-3CR} ($-6.4\text{ }^\circ\text{C}$) are lower than that of P1_{ADMET} and P2_{ADMET}. This difference can be explained by the presence of double bonds in the backbone of P1 and P2 that limits the chain mobility and thus decreases the T_g . Nevertheless, in all cases the T_g values were below the human body temperature, thus the polymers are being in a rubber state and possessing potential biomedical applications.^[22]

DMA was performed on the polymer that possesses the highest “biomass-derived” carbon % and the highest T_g (P2_{ADMET}). The thermomechanical properties of this sample were determined by a temperature sweep experiment between -5 and $45\text{ }^\circ\text{C}$ employing a traction set up, and using a frequency of 1 Hz

and strain amplitude of 5% (Figure S25, Supporting Information). The storage modulus E' in the glassy state was around 558 MPa . When increasing the temperature, the decrease of the E' value indicates a transition from a glassy state to a rubbery state. The alpha transition temperature T_α of this polymer was determined from the maximum of $\tan\delta$ at $22\text{ }^\circ\text{C}$. The beginning of the rubbery plateau can be observed at $45\text{ }^\circ\text{C}$. Interestingly for the biomedical applications aimed at $37\text{ }^\circ\text{C}$, which is even above the T_α , the E' value remained relatively high (0.6 MPa).

Next, primary chondrocytes from human nasal septum were selected to evaluate the cytotoxicity of the P2_{ADMET} since these cells are the predominant cell type responsible for cartilage formation, and they are recognized as a potential source to create cartilage implants with autologous cells. The ethics approval was reviewed and approved by the Ethics Committee of the Medical Faculty Mannheim of Heidelberg University (ethics approval number: 2018-507N-MA). Written informed consent was obtained from all donors. In order to evaluate possible cytotoxic effects on chondrocytes of the polymer, the elution assay to identify potential soluble cytotoxic substances was performed according to the specifications of DIN EN 10993-5 with modifications (Figure 3). To investigate the direct interaction of the polymer surface with cells, the direct contact test was performed after 24 and 72 h exposure of P2_{ADMET} to chondrocytes. The tested eluates displayed no effect on the viability of the chondrocytes. In contrast, after an incubation of 72 h, the viability of the cells had

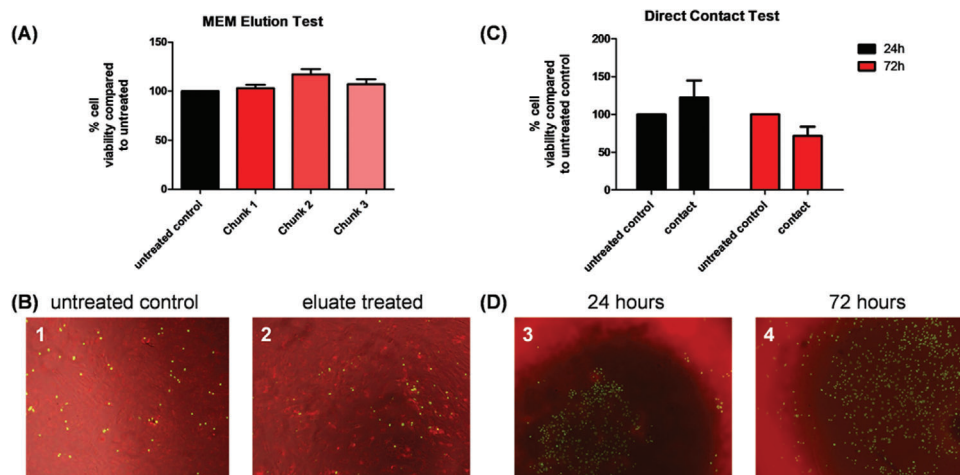


Figure 3. Investigation of effects on the cell viability of eluates of the polymer (MEM Elution Test) and the polymer in direct contact with cells (Direct Contact Test). A) Generated eluates of P2_{ADMET} did not affect the cell viability of chondrocytes. The cell viability was determined using the alamarBlue Assay. B) Chondrocytes in normal media or treated with eluates were stained with fluorescent dyes, i.e., for dead cells with SytoxGreen (green) and with ATP-Red for live cells (red). No differences in the distribution of the dead cells were observed (B1 and B2). C) The viability of the chondrocytes was investigated after 24- and 72-h incubation with polymer chunks (Direct Contact Test) using the alamarBlue assay. No effects were observed after 24 h, but after 72 h, the viability had decreased to 71% compared to the viability of the untreated cells. D) Chondrocytes in direct contact with the polymer were stained with SytoxGreen after 24- and 72-h incubation to indicate dead cells (green). The number of dead cells (green) was increased after 72 h (D3) compared to 24 h (D4). The red color indicates autofluorescence at the edge of the polymer.

decreased to 71% compared to the untreated control. Nevertheless, the cell viability was higher than 70%, thus, P2_{ADMET} could be considered biocompatible according to the specifications of DIN EN 10993-5.

We investigated the hydrophobicity of the novel polymer P2_{ADMET} by static contact angle test in water as probe liquid, because the functional groups on the surface of the polymer could play an important role in the interactions among materials with biological molecules and cells.^[23] Accordingly, P2_{ADMET} showed water contact angle of $\approx 80^\circ$ (refer to Figure 2E). It is generally agreed that hydrophilic surfaces have contact angle with water in the range 1–30° and those of hydrophobic surfaces are $>90^\circ$.^[24] Thus, P2_{ADMET} showed values somewhere between these ranges, suggesting a slightly hydrophilic polymer compared to the previously reported isosorbide-based polyester derivatives,^[25] so, the data is consistent with the presence of polar α -acyloxy amides functionalities.

3. Conclusion

By taking advantage of the toolbox of isosorbide derivatives in addition to the synergy of MCRs and metathesis chemistry, the synthesis of bio-based functional isosorbide polymers (i.e., polyesters) decorated with α -acyloxy amide motif was accomplished. The P-3CR was employed either as a direct polymerization approach or as a handle for the synthesis of novel isosorbide monomers accessible for a further ADMET polymerization. The chemical structure of the polyesters that are not accessible by any other conventional methodologies was characterized in-depth via NMR, SEC, and ATR-IR. The “biomass-derived” carbon % of the polymers varied between 66.2 and 76.9; the polymers were isolated with reasonable molecular weight in high yields. In addition, the thermal properties of the novel isosorbide-based poly-

mers were investigated via TGA and DSC. Particularly, the DSC studies indicated that the polymers were in the amorphous state, being characterized by T_g values below the human body temperature. The mechanical properties and the biocompatibility of the functional novel polyester derivative with the highest “biomass-derived” carbon % were evaluated via DMA and cytotoxicity test. The exemplary P2_{ADMET} was biocompatible with the chondrocyte cells under the conditions used in the tests. In summary, the work described herein highlights the complementary nature of isosorbide derivatives with MCRs and metathesis chemistry to illustrate the potential utility of isosorbide as a building block for polymers with prospective biomedical application (namely, as novel cartilage materials).

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

Acknowledgements

H.M. acknowledges continued support from the Karlsruhe Institute of Technology (KIT) in the context of the MSE program of the Helmholtz Association. Prof. M.A.R. Meier, Prof. C.M. Niemeyer, and Prof. P. Levkin, respectively, are acknowledged for the access of diverse analytical characterization facilities. B. Huber (SML) is also acknowledged for the continuous support for the SEC measurements. The authors acknowledge Emmanuel Ibarboure from the Laboratory of Organic Polymer Chemistry (LCPO) for his help with Dynamic Mechanical Analyses (DMA).

Open access funding enabled and organized by Projekt DEAL.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the Supporting Information of this article.

Keywords

acyclic diene metathesis, isosorbide, multicomponent reactions, poly(ester)s decorated with α -acyloxy amides

Received: December 21, 2021
Revised: May 11, 2022
Published online: June 10, 2022

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